grading. DKI-based model predictions were significantly correlated with progression-free survival.

IMG-15. PEDIATRIC GLIOBLASTOMAS CONTRAST ENHANCEMENT PATTERN IS PREDICTIVE OF SURVIVAL Zsila Sadighi, <u>Halyna Pokhylevych</u>, Maria Gule-Monroe, Melissa Chen, Greg Fuller, Stephen Gruschkus, David Sandberg, Susan McGovern, Mary Frances McAleer, Wafik Zaky, Soumen Khatua, and Jason Johnson; The University of Texas MD Anderson Cancer Center, Houston, TX, USA

BACKGROUND: Pediatric GBMs are rare, accounting for 3% of all pediatric CNS tumors. Despite advances in treatment, the outcomes for pediatric glioblastomas (GBM) have not significantly improved. Research suggests a link between enhancement patterns and survival in adult patients with glial tumors. We sought to study this relationship in a cohort of pediatric GBMs. METHODS: A radiology database was searched for cases < 22 years, pathology proven brain glioblastoma, and pre-surgical MR imaging available for review. Based on pre-treatment, T1-contrast enhanced MR images, size, and contrast enhancement patterns were characterized as focal, diffuse, or ring-like. The extent of resection was assessed by comparing pre- and post-surgery T2 hyperintensity and contrast enhancement. RE-SULTS: 64 eligible patients (age 2-21y, 14.6 + 5.4) were identified. The majority of lesions demonstrated enhancement on gadolinium-enhanced T1 imaging. (n=58/64; 90%). The lesions were categorized into six (9.4%) cases with focal enhancement, 37 (57.8%) cases with diffuse enhancement, and 15 (23.4%) with ring-like enhancement. Patients who received GTR/subtotal resection (STR) and had focal-enhanced GBMs had a significantly longer progression-free survival (PFS) - 14.1 months (p = 0.0308), comparing to diffuse and ring-like enhancing glioblastomas which had respectively 13.9 and 5.5 months of PFS. DISCUSSION: Our data suggests that the contrast enhancement pattern is a significant prognostic factor for survival in pediatric GBM. Patients with GTR/STR who had focal-enhancing GBMs had a significantly longer progression-free survival (p=0.03) comparing to other enhancement patterns.

## IMG-16. WHOLE TUMOR DIFFUSION KURTOSIS IMAGING ANALYSIS FOR DISCRIMINATING PEDIATRIC POSTERIOR FOSSA TUMORS: ACCURACY AND REPEATABILITY Ioan Paul Voicu<sup>1</sup>, Antonio Napolitano<sup>1</sup>, Alessia Carboni<sup>1</sup>,

Ioan Paul Voicu<sup>1</sup>, Antonio Napolitano<sup>1</sup>, Alessia Carboni<sup>1</sup>, Massimo Caulo<sup>2</sup>, Andrea Carai<sup>1</sup>, Maria Vinci<sup>1</sup>, Evelina Miele<sup>1</sup>, Sabrina Rossi<sup>1</sup>, Antonella Cacchione<sup>1</sup>, Sabina Vennarini<sup>3</sup>, Elisabetta Ferretti<sup>4</sup>, Angela Mastronuzzi<sup>1</sup>, Paolo Tomà<sup>1</sup>, and <u>Giovanna Stefania Colafati<sup>1</sup></u>, <sup>1</sup>Bambino Gesù Children's Hospital, Rome, Italy, <sup>2</sup>Institute for Advanced Biomedical Technologies-ITAB, Chieti, Italy, <sup>3</sup>Santa Chiara Hospital, Trento, Italy. <sup>4</sup>University "La Sapienza", Rome, Italy

PURPOSE: Diffusion kurtosis imaging (DKI) has not yet been tested for pediatric brain tumors. Estimating diffusion values from whole-tumor based (VOI) segmentations may improve diffusion measurement repeatability compared to conventional region-of-interest (ROI) approaches. Our purpose was to compare repeatability between ROI and VOI DKIderived diffusion measurements and to assess VOI-based DKI accuracy in discriminating among pediatric posterior fossa tumors. MATERIALS AND METHODS: We retrospectively analyzed 34 children (19 M, 15F, mean age 7.48 years) with posterior fossa tumors who underwent preoperative 3T MRI including DKI. For each patient, two neuroradiologists independently segmented the whole solid tumor (VOI), the area of maximum tumor diameter and a smallROI.Inter-observer variability was assessed with coefficient of variation (COV) and Bland-Altman plots. VOI-based DKI metrics accuracy in discriminating among tumor histology and for tumor grading were assessed with MANOVA and ROC analyses respectively. Correlation between grading accuracy and inter-observer variability was assessed with Spearman's rho. RESULTS: Tumor histology included medulloblastoma (15), pilocytic astrocytoma (14) and ependymoma (5). VOI-based measurements presented lower variability than ROI-based measurements across all DKI metrics. DKI-derived metrics could accurately discriminate between tumor subtypes (Pillai's trace: p<0.001) and were accurate for tumor grading (AUCs of 0.919, 0.986, 0.996, 0.842 and 0.926 for RK, MK, AK, FA and MD respectively). VOI-based COV was significantly correlated to AUC values (R=-0.900, p<0.037). CONCLUSIONS: DKI-derived metrics are useful for pediatric posterior fossa tumor discrimination and grading. VOI-based diffusion measurements present improved repeatability compared to ROI-based measurements and are significantly correlated to diagnostic accuracy.

IMG-17. RADIOMICS CHARACTERIZATION OF FOUR PEDIATRIC BRAIN TUMOR SUBTYPES IN PDX MOUSE MODELS <u>Natalie Serkova</u>, Marina Stukova, Samuel Henehan, Jenna Steiner, Angela Pierce, Andrea Griesinger, Bethany Veo, Irina Alimova, Sujatha Venkataraman, Adam Green, Nathan Dahl, Nicholas Foreman, and Rajeev Vibhakar; University of Colorado Anschutz Medical Campus, Aurora, CO, USA

BACKGROUND: Previously, we have reported on the development of advanced magnetic resonance imaging (MRI) protocols for mouse brain tumors. The goal of this follow-up pre-clinical study was to develop a machine-learning MRI classifier (radiomics) for four subtypes of childhood brain tumor in patient-derived xenograft (PDX) mice. METHODS: MRI scans on orthotopic medulloblastoma, ependymoma, ATRT and DIPG PDX (each n=12 animals) were performed on the animal 9.4 Tesla scanner with an in-plane resolution of 47 microns. Image segmentation, as well as shape and texture based radiomics descriptors were modeled using a modified COLIAGE software for tumor classification and to characterize tumor habitat of each tumor subtype. RESULTS: The mean tumor volumes were 11.2 mm3. Each MRI scan was segmented into three regions: (i) well defined tumor (including distant metastases); (ii) peritumoral edema; (iii) tumor necrosis. 360 radiomics features (capturing co-occurrence, grey-level dependence and directional gradients) were obtained for each region. The model classified four subtypes with high accuracy while achieving sufficient segmentation accuracy despite the small lesion size. A subset of fourteen tumoral, six peritumoral and five distant MRI radiomics features were found to be predictive of the tumor sub-type (p=0.0017) independently of tumor anatomical location. CONCLUSIONS: MRI protocols followed by radiomics feature analysis discriminated among specific radiological features for four distinct orthotopic PDX models: medulloblastomas exhibit low ADC values, high angiogenesis and cortical metastases as compared to ependymomas (high levels of edema and olfactory bulb metastases), ATRT (the highest level of necrosis) and DIPG (highest T2 signal intensities and spinal metastases).

IMG-18. ASSESSMENT OF SUSPECTED DISEASE PROGRESSION USING MULTIPARAMETRIC 18F-CHOLINE PET/MRI IN CHILDHOOD AND TEENAGE-YOUNG ADULT GLIOMAS Valentina Ferrazzoli, Ananth Shankar, Julia Cockle, Christine Tang, Ahmed Al-khayfawee, Benjamin Thomas, Anna Barnes, Jamshed Bomanji, Francesco Fraioli, and <u>Harpreet Hyare;</u> UCLH, London, United Kingdom

OBJECTIVES: Evaluation of post-treatment glioma burden remains a significant challenge in children, teenagers and young adults (TYA). The aim of this study was to evaluate the utility of ChoPET/MRI for evaluation of suspected disease progression in childhood and TYA gliomas. METHODS: 27 patients (mean age 14 years, range 6-21 years) with suspected glioma disease progression were evaluated with ChoPET/MRI (n=59). Relative cerebral blood volume (rCBV), apparent diffusion coefficient (ADC) and maximum standardised uptake values (SUV $_{\rm max})$  in enhancing (enh) and non-enhancing (ne) tumour and normal-appearing white matter (wm) were For characteristic (ICBV<sub>enb</sub>, rCBV<sub>wm</sub>, ADC<sub>enb</sub>, ADC<sub>w</sub>, ADC<sub>w</sub>, SUV<sub>enb</sub>, SUV<sub>wm</sub>). 2 blinded radiologists scored tumour probability (1 = un-likely, 5 = definitely). Sensitivity and specificity calculated with gold standard histopathology or clinical follow-up. RESULTS: Accuracy for the detection of residual/recurrent tumour on conventional MRI was 96.3% (91.7% ≤14 years, 100% ≥15 years) and ChoPET was 73.1% (66.7% ≤14 years, 80.0% ≥15 years). Lack of agreement was observed in 9/27 patients, with ChoPET superior to MRI in 1 case of a posterior fossa tumour. Tumour component analysis demonstrated significantly higher SUV<sub>enh</sub> and SUV<sub>ne</sub> than SUV<sub>wm</sub> (SUV<sub>enh</sub>: p<0.001; SUV<sub>ne</sub>: p=0.004, equivalent to venh and SV<sup>w</sup>me observed for ADV and rCBV (ADC<sub>enh</sub>, ADC<sub>ne</sub>: p<0.001 vs ADC<sub>wm</sub>; rCBV<sub>enh</sub>, rCBV<sub>ne</sub>: p<0.001 vs rCBV<sub>wm</sub>). CONCLUSIONS: MRI is more sensitive than ChoPET in the evaluation of suspected disease progression in TYA gliomas. However, quanititative ChoPET is able to detect enhancing and non-enhancing tumour and may be helpful in evaluating posterior fossa disease where MRI is equivocal.

IMG-19. RADIOMICS AND SUPERVISED DEEP LEARNING TO PREDICT MOLECULAR SUBGROUPS IN MEDULLOBLASTOMA BASED ON WHOLE TUMOR VOLUME LABELING: A SINGLE CENTER MULTIPARAMETRIC MR ANALYSIS Ioan Paul Voicu<sup>1</sup>, Piero Chiacchiaretta<sup>2</sup>, Massimo Caulo<sup>2</sup>, Evelina Miele<sup>1</sup>, Alessia Carboni<sup>1</sup>, Andrea Carai<sup>1</sup>, Francesca Diomedi-Camassei<sup>1</sup>, Sabrina Rossi<sup>1</sup>, Antonella Cacchione<sup>1</sup>, Giada Del Baldo<sup>1</sup>, Elisabetta Ferretti<sup>3</sup>, Angela Mastronuzzi<sup>1</sup>, Paolo Tomà<sup>1</sup>, and <u>Giovanna Stefania Colafati<sup>1</sup></u>, <sup>1</sup>Bambino Gesù Children's Hospital, Rome, Italy, <sup>2</sup>Institute for Advanced Biomedical Technologies-ITAB, Chieti, Italy, <sup>3</sup>University "La Sapienza", Rome, Italy

PURPOSE: Medulloblastoma (MB) is a complex pathology. Four molecular subgroups have been unveiled (Wingless-WNT, Sonic Hedgehog-SHH, Group 3-G3 and Group 4-G4), characterized by significant differences in patient clinical outcome. We investigated the utility of a radiomic analysis to predict molecular subgroups in patients with MB. MATERIALS

AND METHODS: We retrospectively evaluated 42 patients with histological diagnosis of MB, known molecular subgroup, and diagnostic MRI scan performed in our Institution on a 3 Tesla magnet. For each patient, FLAIR, ADC, T2 and contrast-enhanced MPRAGE sequences were analysed. Solid tumor volumes were segmented semiautomatically. 107 features were extracted for each sequence (Pyradiomics, Python). Features were tested for stability against labelling variations, selecting those presenting Intraclass Correlation Coefficient (ICC)>0.9 across all labelling variations and all sequences. Among the remaining features, relevant features were selected with an all-relevant wrapper algorithm (Boruta, R). Remaining features were used to predict MB subgroup with a Random Forest algorithm(R). The most relevant features were ranked based on Gini index (R). RESULTS: 83/107 features presented ICC >0.9 for all sequences. Boruta selected 10 features. Classification analysis yielded an out-of-bag (OOB) error rate of 0.6%, (99.4% accuracy). The most relevant features for classification were "simple" first-order features such as volume, major axis or shape. CONCLUSION: This radiomic study yielded robust features, which showed high accuracy in predicting the molecular MB subgroups. Random forest algorithms are ideal for multiclass classification (eg. MB subgroups) and are intrinsically suited against overfitting. The most relevant for molecular classification were first-order features.

#### IMG-20. RADIOMIC FEATURES IMPROVE PROGNOSTICATION OVER CONVENTIONAL MR DERIVED QUALITATIVE DESCRIPTORS IN PEDIATRIC SUPRATENTORIAL HIGH GRADE GLIOMA: COMPARISON OF MACHINE LEARNING TECHNIQUES John Lucas<sup>1</sup>, Chih-Yang Hsu<sup>1</sup>, Jared Becksfort<sup>1</sup>, Scott Hwang<sup>1</sup>, Zhaohua Lu<sup>1</sup>, Yichuan Wang<sup>2</sup>, Jason Chiang<sup>1</sup>, Christopher Tinkle<sup>1</sup>, Amar Gajjar<sup>1</sup>, Thomas Merchant<sup>1</sup>, and Zoltan Patay<sup>2</sup>; <sup>1</sup>St. Jude Children's Research Hospital, Memphis, TN, USA, <sup>2</sup>Yale School of Public Health, New Haven, CT, USA

PURPOSE/OBJECTIVES: Pediatric supratentorial high-grade glioma (stHGG) is a biologically heterogeneous disease defined by unique mutations, natural history and prognosis. Prior work by our group outlined a role for qualitative imaging features in aiding prognostication. We build on that work by evaluating the prognostic utility of radiomic features (RM) when paired with clinical factors. MATERIALS/METHODS: Ninety-one patients age < 21 years with stHGG treated between 1980-2007 were retrospectively reviewed. Prognostic clinical, qualitative imaging (Visually AcceSAble Rembrandt Images, VASARI), and treatment characteristics were evaluated in concert with manual and automatically segmented (DeepMedic), tumorderived semi-quantitative radiomic features (Pyradiomics) extracted from MR images. Prognostic RM were limited to stable imaging features which were subsequently selected using bootstrapped least absolute shrinkage and selection operator (LASSO). Nonparametric descriptive statistics and prognostication model evaluation, incorporating RM and clinical variables, were developed using random forest (RF), Cox proportional hazards (CPH), and deep learning (deepsurv) algorithms and assessed for goodness of fit using (c-index). RESULTS: A subset (N=80) of 386 intensity, shape, and texture derived RM were stable between pre-treatment MR. 28 RM features were independently predictive of survival when compared to models utilizing combinations of clinical, VASARI and had comparable model fit statistics. CPH, RF and deepsurv showed comparable utility in modelling RM features. Combined modelling of clinical, VASARI and RM features using CPH, RF, and deepsurv resulted in c-indices of 0.68, 0.67, 0.68, respectively. CONCLUSION: RM features are stable and independently prognostic. Combined modelling of clinical, VASARI, and RM features improves prognostication in stHGG.

IMG-21. PROSPECTIVE PREOPERATIVE DETERMINATION OF ISOCITRATE DEHYDROGENASE MUTATION IN GLIOMAS USING SPECTRAL EDITING MAGNETIC RESONANCE SPECTROSCOPY Thanh Nguyen<sup>1</sup>, Gerd Melkus<sup>1</sup>, <u>Michael Taccone<sup>2,3</sup></u>, Diana Ghinda<sup>1</sup>, Carlos Torres<sup>1</sup>, Nader Zakhari<sup>1</sup>, John Woulfe<sup>1</sup>, Gerrard Jansen<sup>1</sup>, Ian Cameron<sup>1</sup>, Ioana Moldovan<sup>1</sup>, and Fahad Alkherayf<sup>1</sup>; <sup>1</sup>The Ottawa Hospital, Ottawa, ON, Canada, <sup>2</sup>Division of Neurosurgery, Department of Surgery, University of Ottawa, Ottawa, ON, Canada, <sup>3</sup>Arthur & Sonia Labatt Brain Tumour Research Centre, The Hospital for Sick Children, Toronto, ON, Canada

BACKGROUND: Gliomas are the most common malignant brain tumors in children and adults. A subset of these tumors harbour mutations in the enzyme isocitrate dehydrogenase (IDH) which produces the novel oncometabolite 2-bydroxyglutarate (2HG). In general, patients with an IDH mutant glioma have a longer survival—often necessitating more re-treatment sessions over the span of a patient's life and surveillance monitoring for tumor recurrence. The need to non-invasively detect early evidence of tumor recurrence is therefore heightened in this unique subset of patients with extended survival. As magnetic resonance spectroscopy (MRS) has been demonstrated to measure biochemical components of intracranial tumors using MRI, we conducted a study in 58 pre-operative adult patients to determine if a diagnosis of IDH mutant glioma could be made confidently using imaging data. METHODS: Patients underwent neuroimaging for diagnosis or preoperative planning on a 3 tesla MR scanner. A MEGA-PRESS spectral editing technique was employed. Imaging findings were directly compared to post-operative histopathologic diagnosis. RESUTLS: For all patients with gliomas from grade II to IV, detection of 2-HG with MEGA-PRESS sequence had a sensitivity between 48% and 81%, specificity between 60% and 100%, PPV between 53% and 100% and NPV between 77% and 85% depending on the CRLB threshold. Among the different metabolite ratios, a 2-HG/NAA ratio >0.034 had the highest sensitivity and specificity, 86% and 73% respectively. DISCUSSION: Magnetic resonance spectroscopy (MRS) is an underused advanced MR technique that deserves consideration in pediatric neuro-oncology given its utility in non-invasively detecting malignant gliomas.

### IMG-22. A DEEP LEARNING MODEL FOR AUTOMATIC POSTERIOR FOSSA PEDIATRIC BRAIN TUMOR SEGMENTATION: A MULTI-INSTITUTIONAL STUDY

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BACKGROUND: Brain tumors are the most common solid malignancies in childhood, many of which develop in the posterior fossa (PF). Manual tumor measurements are frequently required to optimize registration into surgical navigation systems or for surveillance of nonresectable tumors after therapy. With recent advances in artificial intelligence (AI), automated MRIbased tumor segmentation is now feasible without requiring manual measurements. Our goal was to create a deep learning model for automated PF tumor segmentation that can register into navigation systems and provide volume output. METHODS: 720 pre-surgical MRI scans from five pediatric centers were divided into training, validation, and testing datasets. The study cohort comprised of four PF tumor types: medulloblastoma, diffuse midline glioma, ependymoma, and brainstem or cerebellar pilocytic astrocytoma. Manual segmentation of the tumors by an attending neuroradiologist served as "ground truth" labels for model training and evaluation. We used 2D Unet, an encoder-decoder convolutional neural network architecture, with a pre-trained ResNet50 encoder. We assessed ventricle segmentation accuracy on a held-out test set using Dice similarity coefficient (0-1) and compared ventricular volume calculation between manual and model-derived segmentations using linear regression. RESULTS: Compared to the ground truth expert human segmentation, overall Dice score for model performance accuracy was 0.83 for automatic delineation of the 4 tumor types. CON-CLUSIONS: In this multi-institutional study, we present a deep learning algorithm that automatically delineates PF tumors and outputs volumetric information. Our results demonstrate applied AI that is clinically applicable, potentially augmenting radiologists, neuro-oncologists, and neurosurgeons for tumor evaluation, surveillance, and surgical planning.

# **IMMUNOTHERAPY**

#### IMMU-01. IMMUNE CHECKPOINT INHIBITION FOR PEDIATRIC CNS TUMORS: A SINGLE INSTITUTION EXPERIENCE <u>Chantel Cacciotti</u><sup>1</sup>, Jungwhan Choi<sup>2</sup>, Mary Ann Zimmerman<sup>1</sup>, Elise Tierney<sup>1</sup>, Christine Chordas<sup>1</sup>, Jessica Clymer<sup>1</sup>, Susan Chi<sup>1</sup>, and Kee Kiat Yeo<sup>1</sup>; <sup>1</sup>Dana Farber / Boston Children's Cancer and Blood Disorder Center, Boston, MA, USA, <sup>2</sup>Boston Children's Hospital, Boston, MA, USA

INTRODUCTION: Immune checkpoint inhibition through PD-1 and CTLA-4 blockade has shown efficacy in some adult malignancies and is being investigated in pediatrics. We describe our institutional experience with immune checkpoint inhibition in pediatric CNS tumors. METHODS: We performed a retrospective chart review of patients with recurrent, progressive, or refractory pediatric CNS tumors treated with immunotherapy at Dana-Farber/Boston Children's Hospital between 2018–2019. RE-SULTS: Eleven patients were identified, with median age of 11 years (range:3–9). Diagnoses included DIPG (n=3), HGG (n=4), ependymoma (n=1), craniopharyngioma (n=1), HGNET (n=1) and NGGCT (n=1). Eight patients had recurrent disease (5 local; 3 disseminated); three had refractory disease (non-recurrent). Nine patients were treated with combination